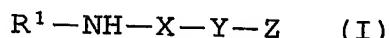


CLAIMS

1. A method for treating a vascular hyperpermeable disease (except macular edema), which method comprises administering
5 to a subject in need thereof a vascular adhesion protein-1 (VAP-1) inhibitor in an amount sufficient to treat said subject for said disease.
2. The method of claim 1, wherein said disease is a disease in
10 mucous membrane.
3. The method of claim 2, wherein said mucous membrane is a mucous membrane of ocular, cutis, otorhinology or respiratory tract.
15
4. The method of claim 1, wherein said disease is aged macular degeneration, aged disciform macular degeneration, cystoid macular edema, palpebral edema, retinal edema, diabetic retinopathy, chorioretinopathy, neovascular maculopathy,
20 neovascular glaucoma, uveitis, iritis, retinal vasculitis, endophthalmitis, panophthalmitis, metastatic ophthalmia, choroiditis, retinal pigment epithelitis, conjunctivitis, cyclitis, scleritis, episcleritis, optic neuritis, retrobulbar optic neuritis, keratitis, blepharitis,
25 exudative retinal detachment, corneal ulcer, conjunctival ulcer, chronic nummular keratitis, Thygeson keratitis, progressive Mooren's ulcer, an ocular inflammatory disease caused by bacterial or viral infection, and by an ophthalmic operation, an ocular inflammatory disease caused by a
30 physical injury to the eye, a symptom caused by an ocular inflammatory disease including itching, flare, edema and ulcer, erythema, erythema exsudativum multiforme, erythema nodosum, erythema annulare, scleredema, dermatitis,

angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

5 5. The method of claim 1, wherein the VAP-1 inhibitor is a compound of the formula (I):

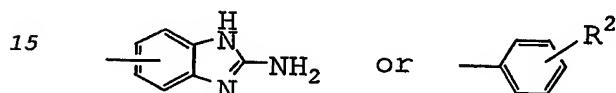


wherein

10 R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or $-\text{CONH}-$; and Z is a group of the formula:



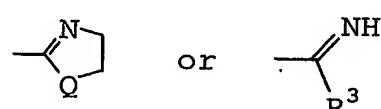
wherein R^2 is a group of the formula: $-\text{A-B-D-E}$

wherein A is a bond, lower alkylene, $-\text{NH-}$ or $-\text{SO}_2-$;

B is a bond, lower alkylene, $-\text{CO-}$ or $-\text{O-}$;

D is a bond, lower alkylene, $-\text{NH-}$ or $-\text{CH}_2\text{NH-}$; and

20 E is optionally protected amino, $-\text{N}=\text{CH}_2$,



wherein

Q is $-\text{S-}$ or $-\text{NH-}$; and

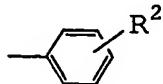
25 R^3 is hydrogen, lower alkyl, lower alkylthio or $-\text{NH-R}^4$ wherein R^4 is hydrogen, $-\text{NH}_2$ or lower alkyl;

or a derivative thereof;

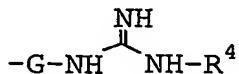
or a pharmaceutically acceptable salt thereof.

30 6. The method of claim 5, wherein, in the formula (I), Z is a

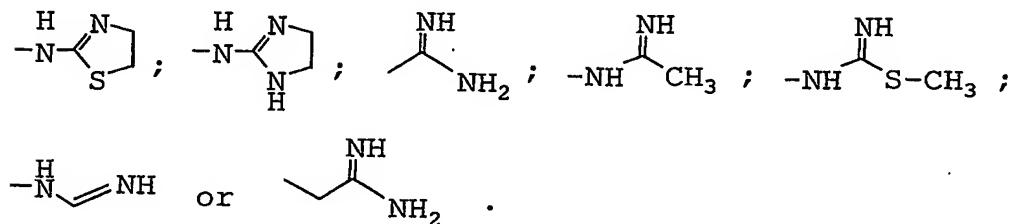
group of the formula:



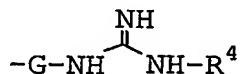
wherein R^2 is a group of the formula:



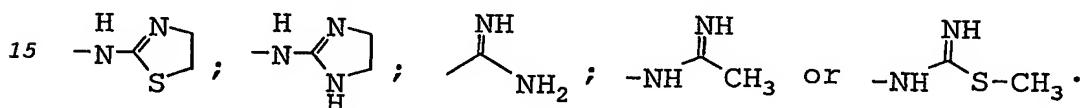
⁵ (wherein G is a bond, $-\text{NHCOCH}_2-$ or lower alkylene and R^4 is hydrogen, $-\text{NH}_2$ or lower alkyl); $-\text{NH}_2$; $-\text{CH}_2\text{NH}_2$; $-\text{CH}_2\text{ONH}_2$; $-\text{CH}_2\text{ON=CH}_2$;



¹⁰ 7. The method of claim 6, wherein, in the formula (I), R^2 is a group of the formula:



(wherein G is a bond, $-\text{NHCOCH}_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-\text{CH}_2\text{NH}_2$; $-\text{CH}_2\text{ONH}_2$; $-\text{CH}_2\text{ON=CH}_2$;



²⁰ methylsulfonylbenzyl.

9. The method of claim 1, wherein the VAP-1 inhibitor is N-{4-[2-(4-[(amino(imino)methyl]amino)phenyl]ethyl}-1,3-thiazol-2-yl}acetamide,

N-[4-(2-{4-[(aminoxy)methyl]phenyl}ethyl)-1,3-thiazol-2-yl]acetamide,

N-[4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide,

5 N-[4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide,

N-[4-[2-(4-{[hydrazino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl]acetamide, or

10 N-(4-{2-[4-(2-{[amino(imino)methyl]amino}ethyl)phenyl]ethyl}-1,3-thiazol-2-yl)acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

10. The method of claim 1, wherein the VAP-1 inhibitor is

15 N-[4-[2-(4-{[amino(imino)methyl]amino}phenyl)ethyl]-1,3-thiazol-2-yl]acetamide;

or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

20 11. A pharmaceutical composition for the treatment of a vascular hyperpermeable disease (except macular edema), which comprises, as an active ingredient, a VAP-1 inhibitor.

12. The composition of claim 11, wherein said disease is a
25 disease in mucous membrane.

13. The composition of claim 12, wherein said mucous membrane is a mucous membrane of ocular, cutis, otorhinology or respiratory tract.

30

14. The composition of claim 11, wherein said disease is aged macular degeneration, aged disciform macular degeneration, cystoid macular edema, palpebral edema, retinal edema,

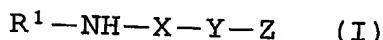
diabetic retinopathy, chorioretinopathy, neovascular maculopathy, neovascular glaucoma, uveitis, iritis, retinal vasculitis, endophthalmitis, panophthalmitis, metastatic ophthalmia, choroiditis, retinal pigment epithelitis,

⁵ conjunctivitis, cyclitis, scleritis, episcleritis, optic neuritis, retrobulbar optic neuritis, keratitis, blepharitis, exudative retinal detachment, corneal ulcer, conjunctival ulcer, chronic nummular keratitis, Thygeson keratitis, progressive Mooren's ulcer, an ocular

¹⁰ inflammatory disease caused by bacterial or viral infection, and by an ophthalmic operation, an ocular inflammatory disease caused by a physical injury to the eye, a symptom caused by an ocular inflammatory disease including itching, flare, edema and ulcer, erythema, erythema exsudativum

¹⁵ multiforme, erythema nodosum, erythema annulare, scleredema, dermatitis, angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

²⁰ 15. The composition of claim 11, wherein the VAP-1 inhibitor is a compound of the formula (I):

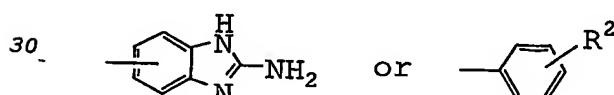


wherein

²⁵ R¹ is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or -CONH-; and Z is a group of the formula:



wherein R² is a group of the formula: -A-B-D-E

wherein A is a bond, lower alkylene, -NH- or -SO₂-;

B is a bond, lower alkylene, -CO- or -O-;
 D is a bond, lower alkylene, -NH- or -CH₂NH-; and
 E is optionally protected amino, -N=CH₂,



5

wherein

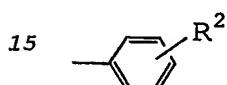
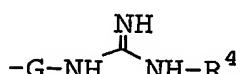
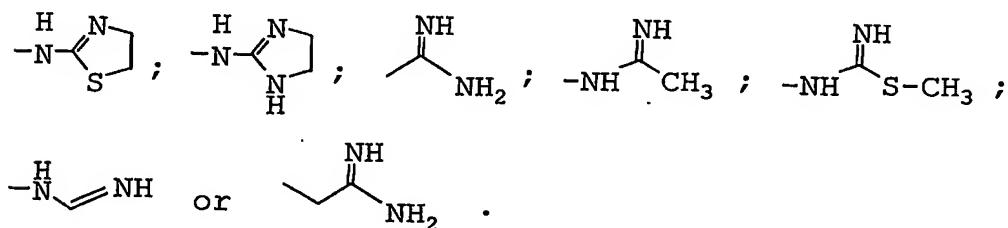
Q is -S- or -NH-; and

R³ is hydrogen, lower alkyl, lower alkylthio or -NH-R⁴ wherein R⁴ is hydrogen, -NH₂ or lower alkyl;

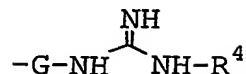
10 or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

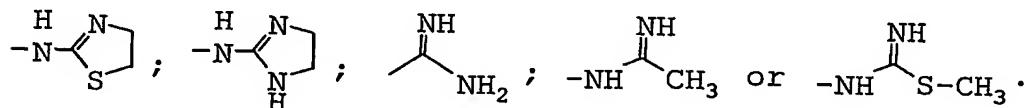
16. The composition of claim 15, wherein, in the formula (I), Z is a group of the formula:

15 wherein R² is a group of the formula:(wherein G is a bond, -NHCOCH₂- or lower alkylene and R⁴ is hydrogen, -NH₂ or lower alkyl); -NH₂; -CH₂NH₂; -CH₂ONH₂;20 -CH₂ON=CH₂;

17. The composition of claim 16, wherein, in the formula (I), R² is a group of the formula:



(wherein G is a bond, $-NHCOCH_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-CH_2NH_2$; $-CH_2ONH_2$; $-CH_2ON=CH_2$;



5

18. The composition of any of claims 15 to 17, wherein, in the formula (I), R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl.

10

19. The composition of claim 11, wherein the VAP-1 inhibitor is

$N-(4-[2-(4-[(amino(imino)methyl]amino)phenyl]ethyl)-1,3-thiazol-2-yl]acetamide$,

15 $N-[4-(2-(4-[(aminoxy)methyl]phenyl)ethyl)-1,3-thiazol-2-yl]acetamide$,

$N-[4-[2-(4-[(amino(imino)methyl]amino)phenyl]ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide$,

20 $N-[4-[2-(4-[(hydrazino(imino)methyl]amino)phenyl]ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide$,

$N-[4-[2-(4-[(hydrazino(imino)methyl]amino)phenyl]ethyl]-1,3-thiazol-2-yl]acetamide$, or

$N-(4-[2-[4-(2-[(amino(imino)methyl]amino)ethyl]phenyl]ethyl)-1,3-thiazol-2-yl]acetamide$;

25 or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

20. The composition of claim 11, wherein the VAP-1 inhibitor is

30 $N-[4-[2-(4-[(amino(imino)methyl]amino)phenyl]ethyl)-1,3-$

thiazol-2-yl}acetamide;
or a derivative thereof;
or a pharmaceutically acceptable salt thereof.

5 21. A use of a VAP-1 inhibitor for preparing a medicament for
the treatment of a vascular hyperpermeable disease (except
macular edema).

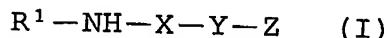
10 22. The use of claim 21, wherein said disease is a disease in
mucous membrane.

23. The use of claim 22, wherein said mucous membrane is a
mucous membrane of ocular, cutis, otorhinology or
respiratory tract.

15 24. The use of claim 21, wherein said disease is aged macular
degeneration, aged disciform macular degeneration, cystoid
macular edema, palpebral edema, retinal edema, diabetic
retinopathy, chorioretinopathy, neovascular maculopathy,
20 neovascular glaucoma, uveitis, iritis, retinal vasculitis,
endophthalmitis, panophthalmitis, metastatic ophthalmia,
choroiditis, retinal pigment epithelitis, conjunctivitis,
cyclitis, scleritis, episcleritis, optic neuritis,
retrobulbar optic neuritis, keratitis, blepharitis,
25 exudative retinal detachment, corneal ulcer, conjunctival
ulcer, chronic nummular keratitis, Thygeson keratitis,
progressive Mooren's ulcer, an ocular inflammatory disease
caused by bacterial or viral infection, and by an ophthalmic
operation, an ocular inflammatory disease caused by a
30 physical injury to the eye, a symptom caused by an ocular
inflammatory disease including itching, flare, edema and
ulcer, erythema, erythema exsudativum multiforme, erythema
nodosum, erythema annulare, scleredema, dermatitis,

angioneurotic edema, laryngeal edema, glottic edema, subglottic laryngitis, bronchitis, rhinitis, pharyngitis, sinusitis, laryngitis or otitis media.

⁵ 25. The use of claim 21, wherein the VAP-1 inhibitor is a compound of the formula (I):

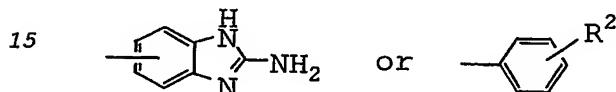


wherein

¹⁰ R^1 is acyl;

X is a bivalent residue derived from optionally substituted thiazole;

Y is a bond, lower alkylene, lower alkenylene or $-CONH-$; and Z is a group of the formula:



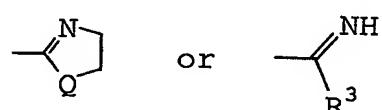
wherein R^2 is a group of the formula: $-A-B-D-E$

wherein A is a bond, lower alkylene, $-NH-$ or $-SO_2-$;

B is a bond, lower alkylene, $-CO-$ or $-O-$;

D is a bond, lower alkylene, $-NH-$ or $-CH_2NH-$; and

²⁰ E is optionally protected amino, $-N=CH_2$,



wherein

Q is $-S-$ or $-NH-$; and

R^3 is hydrogen, lower alkyl, lower alkylthio or

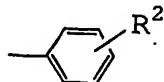
²⁵ $-NH-R^4$ wherein R^4 is hydrogen, $-NH_2$ or lower alkyl;

or a derivative thereof;

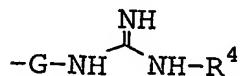
or a pharmaceutically acceptable salt thereof.

³⁰ 26. The use of claim 25, wherein, in the formula (I), Z is a

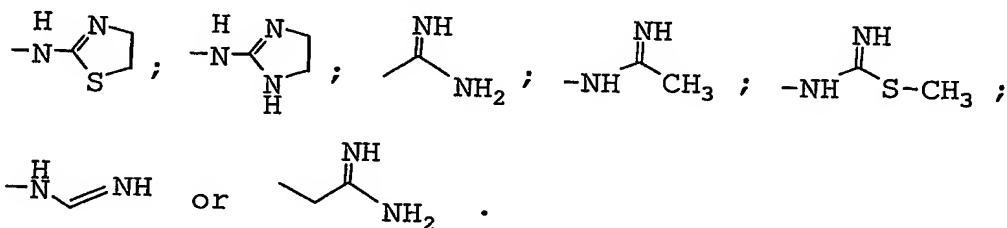
group of the formula:



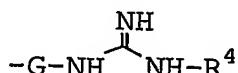
wherein R^2 is a group of the formula:



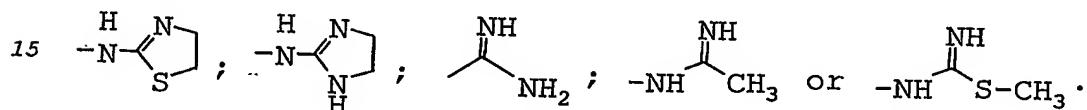
5 (wherein G is a bond, $-\text{NHCOCH}_2-$ or lower alkylene and R^4 is hydrogen, $-\text{NH}_2$ or lower alkyl); $-\text{NH}_2$; $-\text{CH}_2\text{NH}_2$; $-\text{CH}_2\text{ONH}_2$; $-\text{CH}_2\text{ON=CH}_2$;



10 27. The use of claim 26, wherein, in the formula (I), R^2 is a group of the formula:



(wherein G is a bond, $-\text{NHCOCH}_2-$ or lower alkylene and R^4 is hydrogen or lower alkyl); $-\text{CH}_2\text{NH}_2$; $-\text{CH}_2\text{ONH}_2$; $-\text{CH}_2\text{ON=CH}_2$;



28. The use of any of claims 25 to 27, wherein, in the formula (I), R^1 is alkylcarbonyl and X is a bivalent residue derived from thiazole optionally substituted by methylsulfonylbenzyl.

20

29. The use of claim 21, wherein the VAP-1 inhibitor is $\text{N}-\{4-\{2-\{4-\{[\text{amino(imino)methyl]amino}\text{phenyl}\}\text{ethyl}\}-1,3-\text{thiazol-2-yl}\}\text{acetamide}$,

$\text{N}-\{4-\{2-\{4-\{[\text{aminoxy}\text{methyl}]\text{phenyl}\}\text{ethyl}\}-1,3-\text{thiazol-2-}$

yl]acetamide,

N-[4-[2-(4-[[amino(imino)methyl]amino)phenyl]ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide,

N-[4-[2-(4-[[hydrazino(imino)methyl]amino)phenyl]ethyl]-5-[4-(methylsulfonyl)benzyl]-1,3-thiazol-2-yl]acetamide,

N-[4-[2-(4-[[hydrazino(imino)methyl]amino)phenyl]ethyl]-1,3-thiazol-2-yl]acetamide, or

N-(4-{2-[4-(2-[[amino(imino)methyl]amino)ethyl]phenyl}ethyl)-1,3-thiazol-2-yl]acetamide;

10 or a derivative thereof;

or a pharmaceutically acceptable salt thereof.

30. The use of claim 21, wherein the VAP-1 inhibitor is

N-[4-[2-(4-[[amino(imino)methyl]amino)phenyl]ethyl]-1,3-thiazol-2-yl]acetamide;

15 or a derivative thereof;

or a pharmaceutically acceptable salt thereof.